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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,199	10/21/2003	Igor Astsaturov	API-02-13-US	3672

7590 06/19/2009

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
06/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,199	ASTSATUROV ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,11-15,18-26 and 28-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7,11-15,18-26 and 28-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/21/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 30, 2009 has been entered.

Claims 2-3, 8-10, 16, 17, and 27 are cancelled. Claims 1, 11, 12, 14, 18-23, and 28 are amended. Claims 29-34 are newly added. Claims 1, 4-7, 11-15, 18-26, and 28-34 are pending and currently under examination.

This application 10/690,199 filed on Oct. 21, 2003 claims benefit of provisional application 60/420,425 filed on Oct. 22, 2002. The publication number of this application 10/690,199 is US 2004/0223949 A1, published on Nov. 11, 2004.

Claim Objection

2. Previous objection of claims 11-14 and 23 to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, is ***withdrawn*** because the claims 11-14 and 23 have been amended to recite "melanoma-associated tumor" antigen, which is recited in claim independent claim 1.

Claim Rejection – 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 11, 12, and 18-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) Claims 18-22 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's arguments filed 03/30/2009 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on page 4 of the office action mailed on 10/28/2008.

Applicant argues claim 1 has been amended to recite "at least 10 MU/m^2/day", which is also recited in claims 18-22. However, claims 18-22 remain unclear in the following two aspects. First, claims 18-22 recite amended limitation "The method of claim 1 wherein in step a) INF-α2b ---". However, the step a) of claim 1 does not involve administration of INF-α2b. Second, simultaneous recitation of the limitation "at least 10 MU/m^2/day" and the limitation "at least x times per week for ate least x weeks" in claims 18-22 is unclear because, to the Examiner's best understanding of the phrase "at least 10 MU/m^2/day", it means "at least 10 MU (mega unit) per m^2 per day". However, the additional limitation "at least --- *times* per week for at least --- weeks" appears to indicate that the administration is not conducted on a daily basis (i.e. not at least 10 MU (megaunit) per m^2 per day). In this regard, the specification discloses a related phrase "20 MU/m2/d IV 5 days/weekx4 weeks", which appears to mean "20 MU/m^2/day, IV injection, 5 days/week for 4 weeks" accordingly to the cited reference authored by Kirkwood

et al. *J. Clin. Oncol.*, 14:7-17, 1996 (See paragraph [0072], US 2004/0223949, publication of instant application). Applicant should clarify on the record what the limitation "at least 10 $MU/m^2/day$" is supposed to mean in the context of "at least --- *times* per week for at least --- weeks".

(ii) Claims 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 recite "a modified gp100". The metes and bounds of "a modified gp100" cannot be determined because every amino acid residue of gp100 protein can be modified by, for instance, deletion, addition, replacing with any other amino acid residues. Therefore, the identity of "a modified gp100" is indefinite.

(iii) Claims 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites "wherein the melanoma-associated_tumor antigen is selected from the group consisting of gpl00, MART-I/Melan A, gp75/TRP-I, tyrosinase, NY-ESO-I, melanoma proteoglycan, a MAGE antigen, a BAGE antigen, a GAGE antigen, a fragments thereof, and a derivative thereof".

Claim 12 recites "wherein the melanoma-associated_tumor antigen is selected from the group consisting of gpl00, MAGE-I, MAGE-2, MAGE-3, MAGE-4, MAGE-6, MAGEI2, MAGE-51, GAGE-I, and GAGE-2".

It is noted that the specification and the status of art support that a NY-ESO-1 antigen, a MAGE antigen, a BAGE antigen, and a GAGE antigen, recited in amended claim 11 and 12 are tumor antigens. However, the specification and the status of art do not support that a NY-ESO-1 antigen, a BAGE antigen, and a GAGE antigen, recited in amended claim 11 and 12 are melanoma-associated tumor antigens. In the art, a NY-ESO-1 antigen, a BAGE antigen, and a GAGE antigen are not considered as tumor-specific antigen since they are expressed in various normal tissues including testis and placenta (See Table 1, page 302, Vujanovic et al., *J Cell Biochem.* 102(2):301-10, 2007). There is no evidence in the specification or in the art supports that a NY-ESO-1 antigen, a BAGE antigen, and a GAGE antigen are "melanoma-associated antigen" as recited in claims 11 and 12. This issue has been discussed on page 10 of the office action mailed on 01/07/2008, as well as on pages 8-9 of the office action mailed on 10/28/2008, see the teachings by Vujanovic et al., 2007 (See Table 1, page 302, Vujanovic et al., Melanoma cancer vaccines and anti-tumor T cell responses. *J Cell Biochem.* 102(2):301-10, 2007) and Flad et al., 1998 (Flad et al., Direct identification of major histocompatibility complex class I- bound tumor-associated peptide antigens of a renal carcinoma cell line by a novel mass spectrometric method, Cancer Res. 58(24):5803-11., 1998)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

4. Claims 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

The amended claim 11 recites "wherein the melanoma-associated tumor antigen is selected from the group consisting of gp100, MART-I/Melan A, gp75/TRP-I, tyrosinase, NY-ESO-I, melanoma proteoglycan, a MAGE antigen, a BAGE antigen, a GAGE antigen, a fragments thereof, and a derivative thereof". The amended claim 12 recites "wherein the melanoma-associated tumor antigen is selected from the group consisting of gp100, MAGE-I, MAGE-2, MAGE-3, MAGE-4, MAGE-6, MAGEI2, MAGE-51, GAGE-1, and GAGE-2".

No support can be found in the specification that a NY-ESO-1 antigen, a BAGE antigen, a GAGE antigen recited in amended claim 11 and 12 are melanoma-associated tumor antigens. The status of art indicates that a NY-ESO-1 antigen, a BAGE antigen, and a GAGE antigen are not tumor specific antigens, and they are expressed in normal testis and placenta tissue. Accordingly, there is no evidence in the specification or in the art supports that a NY-ESO-1 antigen, a BAGE antigen, and a GAGE antigen are "melanoma-associated antigen" as recited in claims 11 and 12.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly

conveyed to those skilled in the art at the time the application was filed. If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure" (emphasis added).

5. Previous scope of rejection of claims 1, 4-7, 11-15, 18-26, and 28 under 35 U.S.C. 112, first paragraph, because the specification, is ***withdrawn*** because Applicant's arguments have been fully considered and found persuasive.

The withdrawn scope of enablement stated that the specification while being enabling for treating melanoma in a host by administration to a host a polynucleotide encoding a melanoma-associated antigen, which comprises antigenic determinants that induce immune response, followed by multiple administration of interferon-α2b at 20 MU/m^2/day, 5 days/week for 4 weeks, wherein said administrating of the polynucleotide and subsequent administration of interferon-α2b result in an increased T cell response in the host relative to the T cell response that occurs following administrating of the polynucleotide alone, **does not** reasonably provide enablement for treating melanoma by administration of 1) any tumor antigen other than melanoma-associated antigen, or 2) subsequent administration of any interferon other than interferon-α2b, or 3) administration of interferon-α2b (INF-α2b) at any dose for any regimen. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to perform the invention commensurate in scope with these claims.

The first two aspects of non-enabled embodiments of the rejection become *moot* because claim 1 filed on 03/30/2009 recites "melanoma-associated tumor antigen" in step (a) and "interferon-α2b" in step (b). The third aspect of non-enabled embodiments of the rejection is withdrawn because Applicant's arguments that the experimentation involved in the dose regimen is not undue (See page 8 of Applicant's remark filed on 03/30/2009) have been fully considered and found persuasive.

Claim Rejection – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 4-7, 11, 12, 14, 15, 18-23, and 28-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Paoletti** (U.S. patent number 5,942,235; issued on August 24, 1999; this reference has been cited in the office action mailed on 07/25/2006) in view of **Kirkwood et al.** (Kirkwood et al. High-dose interferon alfa-2b significantly prolongs relapse-free and overall survival compared with the GM2-KLH/QS-21 vaccine in patients with resected stage IIB-III

melanoma: results of intergroup trial E1694/S9512/C509801. *J Clin Oncol.* 19(9): 2370-80, 2001; this reference has been cited in the office action mailed on 07/25/2006), and **Aarts et al.** (Aarts et al., Vector-based vaccine/cytokine combination therapy to enhance induction of immune responses to a self-antigen and anti-tumor activity, *Cancer Res.* 62(20):5770-7, 2002).

Claim 1 is directed to a method for treating melanoma comprising: a) administering to a host a composition comprising a nucleic acid encoding a melanoma-associated tumor antigen such that the host develops an immune response against the tumor antigen; and,
b) subsequently administering at least 10 MU/m^2/day interferon alpha 2b (IFN-α2b) to the host; whereby the combination of steps a) and b) provides an enhanced T cell response in the host relative to that which occurs following step a) alone.

Claim interpretation: The limitation "a composition comprising a nucleic acid encoding a melanoma-associated tumor antigen" recited in claim 1 does not exclude other component in the composition in addition to a nucleic acid encoding a melanoma-associated tumor antigen. The limitation "the melanoma tumor antigen is a modified gp100" recited in claim 23 is interpreted as any melanoma tumor antigen (See more discussions on the phrase "a modified gp100" of rejection of claim 23 under 35 USC 112 second paragraph).

Paoletti teaches attenuated recombinant viruses containing DNA coding for a cytokine and/or a tumor associated antigen, as well as methods and compositions employing the viruses. Paoletti teaches that the recombinant viruses can be NYVAC or ALVAC recombinant viruses. The DNA can code for at least one of: human melanoma-associated antigen (MAGE-1; MZE-2) ; IL-2; IFNγ; IL-4; GMCSF; IL-12; B7; erb-B-2, and carcinoembryonic antigen (CEA). Paoletti teaches that the recombinant viruses and gene products are useful for cancer therapy

(See abstract, and lines 40-45, column 13, Paroletti). Paoletti teaches that immune responses in a mammalian host against tumor cells are mediated by T-cells, particularly cytotoxic T lymphocytes (CTLs); white blood cells capable of killing tumor cells and virus-infected cells (column 7, lines 55-57). Furthermore, Paoletti teaches the administration of a cytokine secreted from modified tumor cells can subsequently be utilized for active immunization. The therapeutic potential for such an administration is based on the ability of cytokines to alter the presentation of TAAs to achieve systematic anti-tumor activity (See column 16, lines 3-8). Paoletti teaches that the vaccines or compositions can be co-administered or *sequentially* administered with other anti-neoplastic, anti-tumor or anti-cancer agents and/or with agents which reduce or alleviate ill effects of antineoplastic, anti-tumor or anti-cancer agents; again taking into consideration such factors as the age, sex, weight, and condition of the particular patient, and, the route of administration (See line 55-616, column 13, Paroletti)

Paoletti also teaches (1) viral vectors including poxvirus, vaccinia virus, and avipox virus (See, for instances, column 2, background of the invention, second paragraph; claims 1-8); NYVAC, ALVAC, and TROVAC based recombinant viruses expressing TAAs plus or minus specific cytokines for adoptive immunotherapy (See column 15, lines 45-48, column 17, lines 8-9); as well as canarypox virus (column 16, line 55) and fowlpox virus (column 16, line 64); (2) expression of tumor antigens --- CEA, carcinoembryonic antigen, (columns 70-77, example 17); p53 (columns 65-68, example 15); MAGE-1 (columns 68-70, example 16); and cytokines --- human INFγ (columns 83-84, example 21), IL-2 (column 79-80, example 19) in both ALVAC-based viral vectors (which encompasses ALVAC or ALVAC(2) recited in claim 29-34 of instant application), and NYVAC based viral vectors.

Paoletti does not explicitly teach subsequently administering at least 10 MU/m2/day INF-α2b recited in step (b) of claim 1 for cancer vaccine regimen.

With regard to administering at least 10 MU/m^2/day INF-α2b recited in step (b) of claim 1, and various vaccination of 10 MU/m2/day INF-α2b recited in claims 18-22, 28, and 29, **Kirkwood et al.** teach high dose INF-α2b in the treatment of patients with melanoma. Specifically, Kirkwood et al. teach high dose of INF-α2b (20 megaunits [MU]/m^2/d IV (intravenously) X 5 days a week for four week and 10 MU/m^2 SC (subcutaneously) three times per week [TIW] X 48 weeks), which was approved as adjuvant therapy for high-risk melanoma by the United States Food and Drug Administration (FDA) in 1995 (See first paragraph of Introduction, Kirkwood et al., 2001). The treatment significantly prolongs relapse-free survival and overall survival in high-risk melanoma patient. Kirkwood et al. teaches that dose reduction in the INF-α2b was performed in accordance with the common toxicity criteria established by the National Cancer Institute Treatment Evaluation Program. If criteria dictating dose modification were met, then treatment was withheld until recovery from toxicity. Treatment Statistical Analysis was resumed with a 33% dose reduction after the first treatment interruption for toxicity; a 66% dose reduction (i.e. at least 6 MU/m2/day INF-α2b as recited in claim 29 of instant application) was required after a Efficacy comparisons between the GMK and IFNu2b arms were second treatment interruption for toxicity (See bridging paragraph, page 2371-2372, Kirkwood et al., 2001). However, Kirkwood et al. do not teach combining high dose INF-α2b cytokine therapy with expression of a tumor antigen as a potent treatment of cancers.

With regard to subsequent administering a cytokine recited in step (b) of claim 1, **Aarts et al.** teaches vector-based vaccine/cytokine combination therapy to enhance induction of immune responses to a self-antigen and anti-tumor activity (See title and abstract, Aarts et al., 2002). Aarts et al. teaches various vaccination regimen starting with prime (i.e. initial) administration of a composition comprising a nucleic acid encoding human tumor antigen, carcinoembryonic antigen (CEA), expressed from a recombinant vaccinia (rV) vector such that the host develops an immune response against human CEA, followed by multiple subsequent booster vaccinations, which comprise administration of recombinant cytokines including recombinant GM-CSF and IL-2 (See Materials and Methods, and Table 1, Aarts, et al., 2002).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention to substitute the cytokine (including INFγ and IL-2) taught by Paoletti and Aarts et al. in treating melanoma with a high dose INF-α2b taught by Kirkwood et al., and to follow the cancer vaccination treatment regimens taught by Aarts et al. and Kirkwood et al. to arrive at the claimed inventions of a method of treating melanoma as recited in claims 1, 4-7, 11, 12, 14, 15, 18-23, and 28-34 of instant application.

One having ordinary skill in the art would have been motivated to substitute the cytokine (including INFγ and IL-2) taught by Paoletti and Aarts et al. in treating melanoma with a high dose INF-α2b taught by Kirkwood et al., and to follow the cancer vaccination treatment regimens taught by Aarts et al. and Kirkwood et al. because Aarts provides a "proof of concept" that potent vaccines and vaccine strategies in combination with cytokines, may be essential to obtain the level of T-cell responses directed against a self-antigen that is necessary to achieve anti-tumor responses (See abstract, Aarts et al., 2002).

There would have been a reasonable expectation of success given (1) combinatory cancer therapy with expression of a tumor antigen and expression of a cytokine (including INFγ) either co-administered or sequentially administered, by the teachings of Paoletti, (2) the results of high dose of INF-α2b in the treatment of melanoma by the teachings of Kirkwood et al to achieve a tumor antigen specific immune response involving enhanced T cell response, and (3) vector-based vaccine/cytokine combination therapy to enhance induction of immune responses to a self-antigen and anti-tumor activity in various treatment regimens, by the teachings of Aarts.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

7. Claim 1, 11-13 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Paoletti** (U.S. patent number 5,942,235; issued on August 24, 1999; this reference has been cited in the office action mailed on 07/25/2006) in view of **Kirkwood et al.** (Kirkwood et al. High-dose interferon alfa-2b significantly prolongs relapse-free and overall survival compared with the GM2-KLH/QS-21 vaccine in patients with resected stage IIB-III melanoma: results of intergroup trial E1694/S9512/C509801. *J Clin Oncol.* 19(9): 2370-80, 2001; this reference has been cited in the office action mailed on 07/25/2006), and **Aarts et al.** (Aarts et al., Vector-based vaccine/cytokine combination therapy to enhance induction of immune responses to a self-antigen and anti-tumor activity, *Cancer Res.* 62(20):5770-7, 2002), as applied to claims 1, 4-7, 11, 12, 14, 15, 18-23, and 28-34 above, and further in view of **Kawakami et al.** (Kawakami et al., US Patent No. 5,844,075, issued on 12/01/1998).

The teachings of Paoletti, Aarts et al., and Kirkwood et al. have been discussed in the preceding section of the rejection of claims 1, 4-7, 11, 12, 14, 15, 18-23, and 28-34 under 35 U.S.C. 103(a) as being unpatentable over Paoletti in view of Kirkwood et al. and Aarts et al.

None of Paoletti, Kirkwood et al. and Aarts et al. teaches gp100 as a melanoma-associated tumor antigen recited in claims 11-13 and 23, and SEQ ID No:2 and SEQ ID No:3 of gp100 recited in claims 24-26.

However, at the time of filing of instant application, the gp100 as a melanoma-associated tumor antigen recited in claims 11-13 and 23, and SEQ ID No:2 and SEQ ID No:3 of gp100 recited in claims 24-26, were known in the art. For instant, **Kawakami et al.** teaches immunogenic peptides derived from melanoma antigen designated gp100, including SEQ ID No: 2 and SEQ ID No: 3 recited in claims 24-26 of instant application (See below for the alignment of SEQ ID No: 2 of instant application with SEQ ID No: 84 of Kawakami et al., and the alignment of SEQ ID No: 3 of instant application with SEQ ID No: 104 of Kawakami et al.).

SEQ ID No: 2

```
RESULT 1
US-08-417-174-84
; Sequence 84, Application US/08417174
; Patent No. 5844075
;  GENERAL INFORMATION:
;    APPLICANT:  KAWAKAMI, YUTAKA; ROSENBERG,
;    APPLICANT:  STEVEN A.
;    TITLE OF INVENTION:  MELANOMA ANTIGENS AND
;    TITLE OF INVENTION:  THEIR USE IN DIAGNOSTIC AND THERAPEUTIC
;    TITLE OF INVENTION:  METHODS
;    NUMBER OF SEQUENCES:  126
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  MORGAN & FINNEGAN, L.L.P.
;      STREET:  345 PARK AVENUE
;      CITY:  NEW YORK
;      STATE:  NEW YORK
;      COUNTRY:  USA
;      ZIP:  10154
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  FLOPPY DISK
;      COMPUTER:  IBM PC COMPATIBLE
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
```

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;      SOFTWARE:  ASCII
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/417,174
;      FILING DATE:  05-APR-1995
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/231,565
;      FILING DATE:  22-APR-1994
;      CLASSIFICATION:  435
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  CAROL M. GRUPPI
;      REGISTRATION NUMBER:  37,341
;      REFERENCE/DOCKET NUMBER:  2026-4124US1
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;      TELEX:  421792
;  INFORMATION FOR SEQ ID NO:  84:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  9
;      TYPE:  amino acid
;      STRANDEDNESS:  Unknown
;      TOPOLOGY:  Unknown
;    MOLECULE TYPE:  Peptide
US-08-417-174-84

  Query Match           100.0%;  Score 45;  DB 1;  Length 9;
  Best Local Similarity  100.0%;  Pred. No. 1e+06;
  Matches    9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 IMDQVPFSV 9
              |||||||||
Db          1 IMDQVPFSV 9
```

SEQ ID No:3

```
RESULT 1
US-08-417-174-104
; Sequence 104, Application US/08417174
; Patent No. 5844075
;  GENERAL INFORMATION:
;    APPLICANT:  KAWAKAMI, YUTAKA; ROSENBERG,
;    APPLICANT:  STEVEN A.
;    TITLE OF INVENTION:  MELANOMA ANTIGENS AND
;    TITLE OF INVENTION:  THEIR USE IN DIAGNOSTIC AND THERAPEUTIC
;    TITLE OF INVENTION:  METHODS
;    NUMBER OF SEQUENCES:  126
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  MORGAN & FINNEGAN, L.L.P.
;      STREET:  345 PARK AVENUE
;      CITY:  NEW YORK
;      STATE:  NEW YORK
;      COUNTRY:  USA
;      ZIP:  10154
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  FLOPPY DISK
;      COMPUTER:  IBM PC COMPATIBLE
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  ASCII
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/417,174
;      FILING DATE:  05-APR-1995
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/231,565
;      FILING DATE:  22-APR-1994
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;      CLASSIFICATION:  435
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;  INFORMATION FOR SEQ ID NO:  104:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  9
;      TYPE:  amino acid
;      STRANDEDNESS:  Unknown
;      TOPOLOGY:  Unknown
;    MOLECULE TYPE:  Peptide
US-08-417-174-104

  Query Match           100.0%;  Score 49;  DB 1;  Length 9;
  Best Local Similarity  100.0%;  Pred. No. 1e+06;
  Matches    9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 YLEPGPVTV 9
              |||||||||
Db          1 YLEPGPVTV 9
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Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to incorporate the teachings of Kawakami et al. regarding the DNA encoding immunogenic peptides derived from melanoma antigen gp100, including SEQ ID No: 2 and SEQ ID No:3 recited in claims 24-26 of instant application, into the combined teachings of Paoletti, Kirkwood et al., and Aarts et al. directing to a method for treating melanoma comprising : (a) administering to a host a comprising a nucleic acid encoding a melanoma-associated tumor antigen such that the host develops an immune response against the melanoma-associated tumor antigen; and (b) subsequently administering at least 10 MU/m^2/day INF-α2b to the host, whereby the combination of step (a) and (b) provides an enhanced T cell response in the host relative to that which occurs of following step (a), to arrive at the claimed inventions as recited in claims 1, 11-13 and 23-26.

One having ordinary skill in the art would have been motivated to incorporate the teachings of Kawakami et al. on the DNA encoding DNA encoding immunogenic peptides

derived from melanoma antigen gp100, including SEQ ID No: 2 and SEQ ID No: 3, into the combined teachings of Paoletti, Kirkwood et al., and Aarts et al. because Kawakami et al. teaches that gp100 is a well-established melanoma tumor antigen and SEQ ID No: 2 and SEQ ID No: 3 are immunogenic to induce anti-melanoma T cells mediated immune response.

There would have been a reasonable expectation of success given (1) combinatory cancer therapy with expression of a tumor antigen and expression of a cytokine (including INFγ) either co-administered or sequentially administered, by the teachings of Paoletti, (2) the results of high dose of INF-α2b in the treatment of melanoma by the teachings of Kirkwood et al to achieve a tumor antigen specific immune response involving enhanced T cell response, (3) vector-based vaccine/cytokine combination therapy to enhance induction of immune responses to a self-antigen and anti-tumor activity in various treatment regimens, by the teachings of Aarts, and (4) generation of cytotoxic T lymphocytes (CTL) immune response by administering nucleic acid encoding gp100, by the teachings of Kawakami et al. (See Example 3)

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

8. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

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/Wu-Cheng Winston Shen/
Patent Examiner
Art Unit 1632